

### **C. Amendments to Drawing Figures**

Replacement drawings for all figures 1 through 9 have been provided wherein the characters are the proper size (e.g. Figure 5) and shaded areas have been removed (e.g. Figure 2) in compliance with 37 CFR §1.84. The Examiner is requested to replace the existing figures with these figures.

Applicant submits that to the best of his knowledge these amendments do not add new matter to the specification.

## **D. REMARKS**

### **I. Regarding the Amendments to the Claims**

Claims 1-4,8-31, 33, 34, 36, 37, 39-48, 50 and 51 have been withdrawn.

Claim 5 has been amended by replacing the term "P(J)<sub>b</sub>(LR<sup>15</sup>)" with "P(J)<sub>b</sub>(L<sup>1</sup>R<sup>15</sup>)" on page 59 line 36; the term "C(L)" has been replaced with "C(L<sup>1</sup>)" on page 59 line 36; the term wherein "R<sup>11</sup>" has been properly replaced with "R<sup>10</sup>" and word "or" has been inserted after the word "moieties" on page 61 line 8.

In addition, the paragraph beginning on line 53 has been replaced with a paragraph wherein the word "or" has been properly inserted after the word "moieties".

Claim 6 has been amended by replacing the word "is" before the word "or" on page 61 line 10 with the phrase "further comprises".

Claim 7 has been amended by replacing the number "5" on page 61 line 14 with the number "6".

Claim 35 has been amended by replacing the word "asaturated" on page 79 line 2 with the phrase "a saturated"; replace the phrase "amino or one thiol reactive" with the word "carbonyl" on page 79 line 5; replace the word "conjugate" with the phrase "hydrazine moiety of the conjugate" on page 79 line 6; replacing the phrase "amino or one thiol reactive" with the word "carbonyl" on page 79 line 6; insert the word "hydrazone" before the word "bond" on page 79 line 7 and insert the phrase "thereby crosslinking the natural or synthetic biomolecule" after the word "bond" on page 79 line 7.

Claim 38 has been amended by inserting the word "second" before the word "natural" on page 80 line 16; inserting the phrase "second natural or synthetic biological" before the word "molecule" on page 80 line 17; inserting the phrase "second natural or synthetic biological" before the word "molecule" on page 80 line 19; insert the phrase "thereby crosslinking the natural or synthetic biomolecule" after the word "bond" on page 80 line 20 and inserting the phrase "second natural or synthetic biological" before the word "molecule" on page 80 line 20.

Applicant submits that to the best of his knowledge these amendments do not add new matter to the specification.

### **II. Regarding Comments and/or Objections by the Examiner**

**Item 1.** Applicant confirms that claims 5-7, 32, 35, 38, 49 and 52 (Group II) are those selected for prosecution in this divisional application.

**Item 2.** Applicant is aware of the inversion of the numbers "2" and "0" in the serial number cited in his response to the Restriction Requirement made April 8, 2004, but is unaware of any other such scrivener's errors. Applicant will be certain to cite the correct serial number in future communications.

**Item 3.** The Examiner has noted several inaccurate citing of paragraphs for replacement in the amendments to the specification section of Applicant's Office action response filed August 9, 2006. In addition, the Examiner has stated that Applicant has not complied with the proper form of such amendments. To assist the Examiner and in compliance with his request Applicant has provided both a marked up and clean version of a substitute specification under 37 CFR §1.125 wherein added matter is shown by underline and deleted matter is shown in strikethrough form. In view of this, Applicant requests that the Examiner enter these amendments to the specification.

Further the Examiner states that the claim for priority set forth in the amendment is improper therefore even if the amendments to the specification had not been objected to they would not have been entered. Applicant has amended this paragraph of the specification stating that the present application is a divisional of patent 6,800,728 which claims priority to provisional patent application serial no.: 60/191,186 as required under MPEP §201.11(III)(A). In view of this Applicant requests that the Examiner enter the amendments.

Further the Examiner states that the amendments to the specification would not have been entered even if they were not objected to because they contained new matter. Specifically amending the specification to change the term "imidazinyl" to "imidazolyl". The Examiner suggests that Applicant may have meant the term "imidazolyl". Applicant agrees and has made this amendment to the specification. In view of this Applicant requests that the Examiner enter the amendments.

Further the Examiner objects to the claim amendments provided in the restriction requirement because they are in improper format. Applicant is resubmitting the amendments to the claims (see above) in proper format with this response to clarify the intended amendments in past responses. In view of this Applicant requests that the Examiner enter the amendments.

**Item 4.** The Examiner notes errors in the sequence listing and requests that Applicant submit a substitute computer readable form copy of the sequence listing, a substitute paper copy of the sequence listing, an amendment directing its entry into the specification and a statement that the contents of the paper and computer readable copies are the same and include no new matter as required by 37 CFR §1.825(a) and (b). Applicant has provided a substitute readable form copy of the sequence listing in two formats (.doc and .txt) on CD, a paper copy of

the sequence listing contained on in the computer readable file on the CD and Applicant offers the statement below in compliance with the Examiner's requests.

Applicants statement: The contents of this sequence listing information recorded in computer readable form is identical to the written, on paper, sequence listing and contains no new matter as required under 37 CFR §1.812(e), §1.821(f), §1.821(g), §1.825(b) and §1.825(d). (This statement also appears on the face of the CD.)

Finally, Applicant requests that the sequence listing be entered into the specification.

**Item 5.** The Examiner objects to the disclosure because the word "limited" is misspelled on page 4 line 27 and because the nucleotide sequence provided on page 51 line 30 is not followed by "SEQ ID NO.: 1". Applicant has amended the specification to correct the spelling of "limited" on page 4 line 27 and inserted the phrase "SEQ ID NO.: 1" after the nucleotide sequence on page 51 line 30. In view of this Applicant requests that the Examiner enter the amendments.

**Item 6.** The Examiner has noted that there are a number of letters missing from words on a variety of pages and has requested that Applicant provide a substitute specification. Applicant has complied with the request and is submitting herewith a marked-up and clean substitute specification.

## **E. PATENTABILITY ARGUMENTS**

### **I. Response to Rejections under 35 U.S.C. §112 second paragraph**

**Item 7.** the Examiner has rejected claims 5, 6, 32, 35, 38, 49 and 52 are rejected under 35 U.S.C. §112 second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. More particularly the Examiner states that the phrase "a derivative thereof" in claims 5, 32, 35, and 38 are indefinite because it is not clear what degree of structural and/or functional similarity is required to be present in a compound of formula II or Va and a second compound in order for the second compound to be considered a derivative of compounds of formulas II or Va. The Examiner further states that while Applicant specification describes examples of derivatives the use of the term "includes" obviates such as a definition. Applicant respectfully disagrees. Applicant has cancelled claim 32 and will discuss this rejection as it applies to claims 5, 6, 35, 38, 49 and 52. As the Examiner is well aware claims have been, and are, interpreted narrowly regardless of the fact that they are supposed to be afforded reasonable breadth based on the Doctrine of Equivalence. Further Applicant has the right to be his/her own lexicographer and define certain terms to clarify their intended meaning within the scope of the claim language. Particularly when there is no definite art recognized meaning that is contrary to that provided by Applicant. Applicant has provided such a definition on page 9 line 26 through page 10 line

24 as noted by the Examiner. To further clarify Applicant's definition of the phrase "a derivative thereof" he has removed the term "includes" in each place it occurred in this definition. Consequently, the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

The Examiner also rejects claim 5 stating that the claim provides two different definitions for the variable "L". In response to this rejection Applicant notes that there was a scrivener's error wherein "L" should have been "L<sup>1</sup>", correspondingly Applicant has amended claim 5 to properly label the variable "L<sup>1</sup>". Consequently the Examiner's rejection is moot and Applicant respectfully requests that this rejection be removed.

Further the Examiner states that claim 5 provides a definition of R<sup>11</sup> but that R<sup>11</sup> does not appear in the structural formula or substituents in the claim. Applicant notes that there was a scrivener's error wherein "R<sup>11</sup>" should have been "R<sup>10</sup>", correspondingly Applicant has amended claim 5 to properly label the variable "R<sup>10</sup>". Consequently the Examiner's rejection is moot and Applicant respectfully requests that this rejection be removed.

The Examiner then states that claims 32, 35 and 38 recite that a method of crosslinking is being claimed but no mention of crosslinking is made in the claim. Claim 32 has been cancelled and claims 35 and 38 amended to more clearly define the crosslinking step of these methods. More particularly, Applicant has incorporate the phrase "thereby crosslinking the natural or synthetic biomolecule" in step ii for each claim. Consequently, the Examiner's rejection is moot and Applicant respectfully requests that this rejection be removed.

Further the Examiner states that claim 32 is indefinite because the conjugate of formula Va does not appear to comprise any amino or thiol moieties with which the amino or thiol reactive moieties on the surface can react. Applicant has cancelled this claim consequently the Examiner's rejection is moot and Applicant respectfully requests that this rejection be removed.

**Item 8.** The Examiner states that claims 5-7, 32, 35, 49 and 52 are objected to because of informalities; at claim 5 there appears what is probably a formula for an alkynyl bond, however, the third bond appears more like an underlining mark. Applicant agrees and would note that one skilled in the art would recognize this mark as a triple bond without confusion, however, in order to comply with the Examiner's request an alternative mark has been used which simulates a triple bond in a more usually recognized form. Applicant has provided a substitute specification that includes the more recognizable triple bond representation for claims 5-7, 35, 49 and 52 in view of the fact that claim 32 has been cancelled. Consequently the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

Further the Examiner states that in claim 5 in the third to the last line the word "or" should be inserted after the second comma in the line. Applicant has amended the specification accordingly. Next the Examiner states that the period is missing in claim 7. Applicant disagrees. The period is provided after the and below the structure. Next the Examiner states that the word "or" should be inserted after R<sup>1</sup> and after R<sup>2</sup> in claim 32. Applicant notes that this claim has been cancelled therefore no amendments to this claim have been made in response to the Examiner's objection. Next the Examiner states that in claim 35 the word "asaturated" should be "a saturated". Applicant agrees and has amended the specification accordingly. Next the Examiner states that in claim 35 the phrase "a-bromoacetamido" appears to be a duplicate. Applicant agrees. Applicant has removed this amendment to the specification. Consequently the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

**Item 9.** The Examiner objects to claims 6 and 7 as being improper dependent form for failing to further limit the subject matter of a previous claim. Applicant agrees and has amended these claims to overcome the Examiner's objections. Consequently, the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

## **II. Response to Rejections under 35 U.S.C. §102(b)**

In order to maintain a rejection under 35 U.S.C. §102 (b) the reference must teach each and every aspect of the claimed invention.

**Item 11.** The Examiner rejects claims 5-7, 32, 35, 38, 49 and 52 under 35 U.S.C. §102(b) as being anticipated by the WO Patent Application 01/70685 stating that this reference is available because the current lack of an acceptable claim for priority under 35 U.S.C. §120. Applicant has amended the specification claiming priority to provisional application serial no.: 60/191,186 filed 22 March 2000. Consequently, this reference is improper based on the corrected and acceptable claim for priority to the provisional application. Therefore, the Examiner's rejections are moot and Applicant respectfully requests that this rejection be removed.

**Item 12.** The Examiner rejects claims 5 and 32 under 35 U.S.C. §102(b) as being anticipated by the WO Patent Application 93/14779, "779". More specifically the Examiner states that 779 teaches a compound which anticipates Applicant's compound of Formula II and formula Va respectively. Formula II and Va provide for a thiol or amino reactive group indicated by the letter "B" bound to R or the six membered ring in claims 5 and 32 respectively. Applicant disagrees and notes that claim 32 has been cancelled consequently this response will address only claim 5. The cited compound of "779" does not comprise this moiety nor does it teach the use of this moiety. In the case of Applicant's invention the presence of a thiol or amino reactive moiety is utilized in one embodiment to bind a biomolecule to the compound of formula II. In addition, formula II comprises a –

NH=C(R<sup>1</sup> R<sup>2</sup>) moiety which is not disclosed or taught by 779. For the Examiner to successfully reject claim 5 he must show that the cited reference teaches each and every aspect of the claimed invention. Based on the above argument it is clear that the reference does not teach or disclosure Applicant's formula. The suggestion by the Examiner that the structure in the cited reference qualifies as a derivative of formula II is improper based on Applicant's definition in the specification. Amendments requested by the Examiner to this section should assist in providing a clearer definition as to what Applicant intends by his use of the term derivative. Consequently, Applicant respectfully requests that this rejection be removed.

**Item 13.** The Examiner rejects claims 5 and 35 under 35 U.S.C. §102(b) as being anticipated by Whelihan (U.S. Patent 6,238,860). More specifically the Examiner states that Whelihan teaches polypeptides which are synthesized with a Glu-Gly-Gly-Gly-Ser spacer sequence, modified with a hydrazide functionality, and then immobilized on an aldehyde-functional methacrylate resin support. He further states that the polypeptide spacer hydrazide reaction product of Whelihan is deemed to be a derivative of Applicant's compound of formula II and Va. Formula II and Va provide for a thiol or amino reactive group indicated by the letter "B" bound to R or the six membered ring in claims 5 and 35 respectively. The cited compound of Whelihan does not comprise this moiety nor does it teach the use of this moiety. In the case of Applicant's invention the presence of a thiol or amino reactive moiety is utilized in one embodiment to bind a biomolecule to the compound of formula II or Va. In addition, formulas II and Va comprise a –NH=C(R<sup>1</sup> R<sup>2</sup>) moiety which is not disclosed or taught by Whelihan. For the Examiner to successfully reject claims 5 and 35 he must show that the cited reference teach each and every aspect of the claimed invention. Based on the above argument it is clear that the reference does not teach or disclosure Applicant's formula. The suggestion by the Examiner that the structure in the cited reference qualifies as a derivative of formula II or Va is improper based on Applicant's definition in the specification. Amendments requested by the Examiner to this section should assist in providing a clearer definition as to what Applicant intends by his use of the term derivative. Consequently, Applicant respectfully requests that this rejection be removed.

**Item 14.** The Examiner rejects claims 5 and 38 under 35 U.S.C. §102(b) as being anticipated by Sivam (U.S. Patent 5,521,290). More specifically, the Examiner states that Sivam teaches derivatizing a monoclonal antibody with sulfhydryl groups, reacting a hydrazide-containing bifunctional linker of formula I with the derivatized monoclonal antibody, and then reacting the monoclonal antibody hydrazide with ricin A which has been oxidized to form aldehyde groups on its saccharide moieties. He further states that the reaction product of the derivatized monoclonal antibody and the bifunctional linker of Sivam is deemed to be a derivative of Applicant's compound of formula II and of Applicant's conjugate of formula Va. In both formulas II and Va wherein A is NH(C=O), NH(C=S), NH(C=NH), NHNH(C=O), NHNH(C=S) all provide a –NH– group between R or

the six membered ring and the  $\text{-NHNH}_2\text{-}$  respectively. This structural element is not taught or disclosed in Sivam. For the Examiner to successfully reject claims 5 and 35 he must show that the cited reference teach each and every aspect of the claimed invention. Based on the above argument it is clear that the reference does not teach or disclosure Applicant's formula. The suggestion by the Examiner that the structure in the cited reference qualifies as a derivative of formula II or Va is improper based on Applicant's definition in the specification. Amendments requested by the Examiner to this section should assist in providing a clearer definition as to what Applicant intends by his use of the term derivative. Consequently, Applicant respectfully requests that this rejection be removed.

### CONCLUSION

In view of the above, Applicant respectfully requests that the Examiner issue an allowance of the claims.

Respectfully submitted,

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